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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,748	10/11/2005	Hiroshi Fukushima	Q86326	2073

23373 7590 03/30/2007  
SUGHRUE MION, PLLC  
2100 PENNSYLVANIA AVENUE, N.W.  
SUITE 800  
WASHINGTON, DC 20037

EXAMINER
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GRAZIER, NYEEMAH

ART UNIT	PAPER NUMBER
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1626

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/30/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	Application No. 10/525,748	Applicant(s) FUKUSHIMA ET AL.	
	Examiner Nyeemah Grazier	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 25 February 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☒ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>2/25/05, 8/10/05</u> | 6) <input type="checkbox"/> Other: _____  |

**DETAILED ACTION**  
**FIRST ACTION ON THE MERITS**

**I. ACTION SUMMARY**

Claim 1 is currently pending.

**II. PRIORITY**

This application is a 371 of PCT/JP03/10828, filed August 27, 2003 and claims benefit under 35 U.S.C. 119 (a-d) to JAPAN 2002-249821, filed August 29, 2002.

**III. INFORMATION DISCLOSURE STATEMENT**

The information disclosure statement (IDS) submitted on February 25, 2005 and August 10, 2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

**IV. REJECTION(S)**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. § 103(a) that forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

*Graham v. John Deere Co.* set forth the factual inquiries necessary to determine obviousness under 35 U.S.C. §103(a). *See Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966). Specifically, the analysis must employ the following factual inquiries:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.

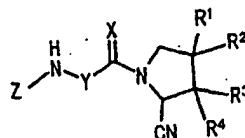
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3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 35 U.S.C. § 103(a) as being obvious over EP 1 333 025 A1, TAISHO Pharmaceuticals (Int'l Application No. PCT/JP01/09818; Int'l Publication No. WO 02/038541) in view of Berge et al., Journal of Pharmaceutical Sciences, Vol. 66, pp. 1-19 (1977). The instant invention is drawn to a benzenesulfonate salt of (2S, 4S)-2-cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine. The pharmaceutical compound is allegedly a dipeptidyl peptidase IV (DPPIV) inhibitor.

**The Scope and Content of the Prior Art (MPEP §2141.01)**

The prior art of record is drawn to cyanopyrrolidine derivatives of Formula (I). The pharmaceutical compound has the same medicinal properties as the instant invention. Namely, it is a DPPIV inhibitor.



The prior art of record is comparable to the instant invention as variables R1 may represent fluoro, R2-R4 may represent hydrogen, X may represent oxygen, Y may represent -CR5R6 wherein R5R6 may each represent hydrogen, and Z may represent (2-hydroxy-1,1-dimethyl)ethyl.

**The Difference Between the Prior Art and the Claims (MPEP §2141.02)**

The difference between the instant invention and the TAISH Pharm., Co. Ltd. publication is in scope. The instant invention is drawn specifically to the benzenesulfonate salt form, while the art of record is drawn to any pharmaceutical salt form. Also, the instant invention is a specie of the subgenus.

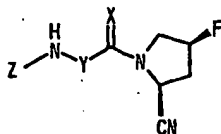
**Resolving Level of Ordinary Skill in the Pertinent Art**

The pertinent art is drug discovery and generally medicinal chemistry. One of ordinary skill in the pertinent art of medicinal chemistry would have the motivation to make and use to instant invention because there is motivation to make in the instant compound in the abovementioned reference, which teach a preferred embodiment that renders the instant invention obvious. Furthermore, the inventions have the same pharmaceutical properties as they are DPPIV inhibitors. The motivation to make claimed compound derives from the expectation that structurally similar compounds are generally expected to have similar properties and have similar utilities. In re Gyurik, 596 F. 2d 1012, 201 USPQ 552 (CCPA 1979).

**Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)**

It is well established that consideration of a reference is not limited to the preferred embodiments or working examples, but extends to the entire disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to a person of ordinary skill in the art. In re Boe, 148 USPQ 507 (CCPA 1966). For an invention to be obvious, two things must be found in the prior art: 1) the suggestion of the invention, and 2) the expectation of success. In re Vaeck, 20 USPQ.2d 1438, 1441 (Fed. Cir. 1991).

The prima facie case for obviousness is derived from the preferred teaching of the references. The reference teaches preferred compounds and preferred variable substituents in the "Best Mode for Carrying Out the Invention." See, TAISHA at pp. 4-5. The preferred subgroup of Formula (I) is Formula (2) below:



The preferred substitution on formula (2) is where X is oxygen (Id. at p. 5, l. 0017), Y is -CH<sub>2</sub> (Id. at p. 5, l. 0018), and Y is -CH<sub>2</sub> and Z is (2-hydroxy-1,1-dimethyl)ethyl (Id. at p. 5, l. 0020).

The expectation of success is derived from the prior art of reference and its preferred embodiment and preferred subgenus. Additionally, the specification of the TAISHO publication teaches how to make the compounds and disclose protocol used to test the compounds for its inhibitory effects. Thus, although the claims are not identical, the prior art of reference suggests the instant invention.

Furthermore, Berge, et al. states that pharmaceutical agents can be manipulated and optimized by salt forms. Benzenesulfonate is cited therein as a commercially marketed salt. Thus, the TAISHO publication in view of the Berge, et al. publication renders the instant invention obvious.

***Provisional Obviousness-Type Double Patenting***

Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 6, 7-10 of copending Application No. 10/416,370. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

A rejection based on nonstatutory double patenting is based on a judicially created doctrine grounded in public policy so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969). See also M.P.E.P. § 804 (2001).

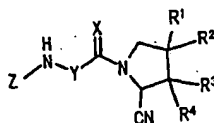
Obvious-type nonstatutory double patenting rejection is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. § 103" with the distinction that the double patent rejection is not considered prior art. Id. See also In re Braithwaite, 379 F.2d 594,

154 USPQ 29 (CCPA 1967). Thus, the analysis employed in an obviousness-type double patent rejection is consistent with a §103(a) analysis set forth in Graham v. John Deere Co., 383 U.S. 1, 148 USPQ 459 (1966). Although the conflicting claims are not identical, they are not patentably distinct from each other.

The instant invention is drawn to a benzenesulfonate salt of (2S, 4S)-2-cyano-4-fluoro-1-[(2-hydroxy-1,1-dimethyl)ethylamino]acetylpyrrolidine. The pharmaceutical compound is allegedly a dipeptidyl peptidase IV (DPPIV) inhibitor.

**The Scope and Content of the Prior Art (MPEP §2141.01)**

The prior art of record is drawn to cyanopyrrolidine derivatives of Formula (I). The pharmaceutical compound has the same medicinal properties as the instant invention. Namely, it is a DPPIV inhibitor.



The prior art of record is comparable to the instant invention as variables R1 may represent fluoro, R2-R4 may represent hydrogen, X may represent oxygen, Y may represent -CR5R6 wherein R5R6 may each represent hydrogen, and Z may represent (2-hydroxy-1,1-dimethyl)ethyl.

**The Difference Between the Prior Art and the Claims (MPEP §2141.02)**

The difference between the instant invention and the co-pending application is in scope. The instant invention is drawn specifically to the benzenesulfonate salt form, while the art of record is drawn to any pharmaceutical salt form. Also, the instant invention is a specie of the subgenus.

**Resolving Level of Ordinary Skill in the Pertinent Art**

The pertinent art is drug discovery and generally medicinal chemistry. One of ordinary skill in the pertinent art of medicinal chemistry would have the motivation to make and

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use to instant invention because there is motivation to make in the instant compound in the abovementioned reference, which teach a preferred embodiment that renders the instant invention obvious. Furthermore, the inventions have the same pharmaceutical properties as they are DPPIV inhibitors. The motivation to make claimed compound derives from the expectation that structurally similar compounds are generally expected to have similar properties and have similar utilities. In re Gyurik, 596 F. 2d 1012, 201 USPQ 552 (CCPA 1979).

**Prima Facie Obviousness-The Rational and Motivation (MPEP §2142-2413)**

It is well established that consideration of a reference is not limited to the preferred embodiments or working examples, but extends to the entire disclosure for what it fairly teaches, when viewed in light of the admitted knowledge in the art, to a person of ordinary skill in the art. In re Boe, 148 USPQ 507 (CCPA 1966). For an invention to be obvious, two things must be found in the prior art: 1) the suggestion of the invention, and 2) the expectation of success. In re Vaeck, 20 USPQ.2d 1438, 1441 (Fed. Cir. 1991).

Furthermore, Berge, et al. states that pharmaceutical agents can be manipulated and optimized by salt forms. Benzenesulfonate is cited therein as a commercially marketed salt. Thus, the co-pending application in view of the Berge, et al. publication renders the instant invention obvious.

Thus, one skilled in the pertinent art would have motivated one skilled in the art to make and use in the instant compounds and compositions with the expectation that they would both have the same pharmacokinetic effect.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application.



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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

#### V. CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nyeemah Grazier whose telephone number is (571) 272-8781. The examiner can normally be reached on Monday through Thursday and every other Friday from 8:30 a.m. - 6:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane, can be reached on (571) 272 - 0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Very truly yours,



Nyeemah Grazier, Esq.

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PRIMARY EXAMINER



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